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Incidence trends and clinical-pathological characteristics of invasive cutaneous melanoma from 1980 to 2010 in the canton of Zurich, Switzerland

Minini, Remo ; Rohrmann, Sabine ; Braun, Ralph ; Korol, Dimitri ; Dehler, Silvia

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Incidence trends and clinical–pathological characteristics of invasive cutaneous melanoma from 1980 to 2010 in the canton of Zurich, Switzerland

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The aims of this paper are to describe the incidence trends of invasive cutaneous melanoma in the Canton of Zurich and to evaluate clinical and pathological factors such as cancer subtype, localization, age and Breslow thickness. A retrospective analysis was carried out with data from the population-based Cancer Registry of Zurich and Zug located in Zurich. A total of 8469 cases in 8034 different patients of invasive cutaneous melanoma were registered for the period 1980–2010 in the Canton of Zurich. Incidence trends were age standardized to the European standard population. Joinpoint regression was used to compute changes in incidence and mortality rates, measured as the annual percent change (APC). The most common subtypes of cutaneous melanoma were superficial spreading melanoma (SSM, 41.1%), followed by nodular melanoma (16.5%), lentigo maligna melanoma (13.5%), acral-lentiginous melanoma (5.0%) and other types of melanoma (2.8%); 21.1% were melanoma not otherwise specified. The trunk was the most frequent location (30.8%), followed by the lower limb and hip (26.4%) and the upper limb and shoulder (22.8%). Statistically significantly increasing incidence trends were observed for both men (APC = 3.0%) and women (APC = 2.1%). Incidences of SSM and melanoma not otherwise specified were the histological subtypes for which a significant increase in incidence was observed (APC for the period 1980–2010 = 3.2% for both). In terms of Breslow thickness, thin melanomas (0.01–1.00 mm) showed an increasing incidence. The incidence of melanoma increased in both men and women between 1980 and 2010. In terms of the different subtypes and Breslow thickness, increasing incidences of the SSM and of thin melanomas (0.01–1.00 mm) were observed. These observations are in agreement with other studies from Southern and Western Switzerland as well as other European countries and the USA. *Melanoma Res* 00:000–000 **Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.**

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Keywords: incidence trends, melanoma, Switzerland, Zurich

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Introduction

Melanoma is a relevant and emerging problem in Switzerland. In 2012, Switzerland was ranked third place among the countries with the highest incidence of melanoma with only Australia and New Zealand had higher incidence rates [1–3]. Assumed risk factors in those two countries are the fair-skinned population, proximity to the equator and ozone layer depletion [4]. There are almost no cases in black and Asian populations, except that they have the same incidence of acral-lentiginous melanoma as Caucasians [1–3,5]. In 2012 in Europe, Switzerland was the country with the highest incidence rates, followed by the Scandinavian countries and the Netherlands [1]. The lowest incidence rates are found in Mediterranean countries because of the darker skin type of the population and different sun-exposure behaviour [1–3]. The incidence is higher among women than among men [1]. Mortality rates are the highest in Norway and Slovenia; Switzerland is ranked sixth [1].

Melanoma is the fourth most common cancer in Switzerland and it has the highest increase in incidence of all cancer types in recent years [6]. The incidence is slightly higher in the French-speaking part of Switzerland, but the incidence in the German-speaking part is increasing and catching up [7]. Early detection leads to increased incidence of thin, but not thick and aggressive, fast-growing melanoma [8]. As a consequence, the mortality rate remains unchanged in Switzerland [6–8] because thin melanomas have a higher survival and a lower mortality rate [8]. Two main risk factors are assumed to be responsible for the increase in the incidences of melanoma in Switzerland and worldwide: increased exposure to the sun and increased dermatological consultations, leading to greater awareness and more consultations. The increased exposure to ultraviolet (UV) radiation can be explained by three main reasons: holidays in sunny/warm destinations, more frequent outdoor activities and increased use of sunbeds [6,8,9].

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Prevention is a highly important factor in reducing the risk of having a melanoma. The most important action is to avoid UV radiation, especially from 10 a.m. to 4 p.m. [6,10]. There are several strategies to protect oneself from UV radiation such as actively seeking shade, covering up and last, but not least, using sunscreen. As the risk of having a melanoma increases with sunburn in childhood, it is highly necessary to avoid it [6,10].

Individuals with a higher melanoma risk than the average population because of a positive family history, one or more melanomas diagnosed in the past or several nevi are recommended to consult a dermatologist and have their integument examined at least every year [10].

The aims of this paper are to describe the incidence trends of the invasive cutaneous melanoma in the Canton of Zurich between 1980 and 2010, and, furthermore, to evaluate changes with respect to clinical and pathological factors such as cancer subtype, localization, age and Breslow thickness.

Patients and methods

A retrospective analysis was carried out with data from the population-based Cancer Registry of Zurich and Zug located in Zurich. A total of 8469 cases of invasive cutaneous melanoma [defined as site C44 using the third edition of the International Classification of Diseases for Oncology (ICD-O-3) [11]] in 8034 different patients were registered for the period 1980–2010 in the Canton of Zurich.

The cancer registry has collected data since 1980. It registers every patient whose registered residence is in the Canton of Zurich and Zug (since 2011) at the point of diagnosis [12].

The histological subtypes were classified using ICD-O-3 codes as follows: superficial spreading melanoma (SSM, 8743), nodular melanoma (NM, 8721), lentigo maligna melanoma (LMM, 8742), acral-lentiginous melanoma (ALM, 8744), other types of melanoma (OTM, 8722, 8723, 8730, 8740, 8741, 8745, 8761, 8770, 8771, 8772, 8780) and melanoma not otherwise specified (MNOS, 8720) [11,13,14].

Tumour localization was classified using ICD-O-3 codes using the following localizations: head and neck (C440–C444), trunk (C445), upper limb and shoulder (C446), lower limb and hip (C447), more than one localization (C448) and unknown localization (C449) [14]. Breslow thickness was classified according to the TNM classification using the following categories: 0.01–1.00; 1.01–2.00; 2.01–4.00; >4.00 and unknown Breslow thickness [15].

Statistical analysis: incidence rates were calculated per 100 000 person-year. All rates are standardized to the European population using the direct method [16]. To assess changes in incidence, we computed the annual percent change (APC) of the standardized rates using joinpoint regression [17,18].

To examine differences in the clinical–pathological characteristics, the Pearson χ^2-test was used to examine differences among the melanoma subtypes for discrete variables such as sex, location, Breslow thickness categories and periods. Furthermore, the Scheffe test was used to compare the median age among the melanoma subtypes. *P*-values less than 0.05 were considered statistically significant. In general, analyses of incidence were carried out at the patient level, whereas calculations of melanoma-specific factors were performed at the case level.

Results

In the period 1980–2010, a total of 8469 documented cases of malignant melanoma were registered in the canton of Zurich by the Cancer Registry of Zurich and Zug.

The most frequent histological subtype was the SSM type (41%), followed by the NM type (16%) and the LMM type (14%). About 21% of all cases were not histologically classified (Table 1). There was a slightly higher incidence among female patients (51.5%) than in male patients (48.5%). Differences in histological subtype and sex were statistically significant ($P < 0.001$), with the biggest difference being observed in the ALM subtype (women 67%), followed by the OTM subtype (women 56%), the NM subtype (men 55%) and the SSM subtype (women 53%).

LMM had the highest median age at diagnosis (70 and 72 years, respectively) and SSM had the lowest median age at diagnosis (55 years). Differences between the mean and the median age and histological subtype were statistically significant ($P < 0.001$) (Table 1).

Most melanomas were located on the trunk (31%), followed by the lower limb and hip (26%), upper limb and shoulder (23%) and head and neck (18%) (Table 1). There were statistically significant differences between location and histological subtype ($P < 0.001$). About 50% of the head and neck melanomas were of the LMM subtype, whereas ALM and OTM subtypes were most frequently located on the lower limb, and the trunk was the preferred location for SSM, NM and MNOS.

About 60% of all skin melanoma cases had a Breslow thickness of 0.01–1.00 mm. A Breslow thickness of 0.01–1.00 mm was the most frequent in all of the subtypes, except for NM, for which it was 2.01–4.00 mm (Table 1). Almost half of all melanoma cases (46.3%) were registered in the period from 2001 to 2010, about one-third (31%) from 1991 to 2000 and about a fifth (22.67%) from 1980 to 1990 (Table 1).

APC and corresponding *P*-values were computed for the periods 1980–2010, 1980–1990, 1991–2000 and 2001–2010.

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Table 1 Clinical–pathological characteristics of melanoma patients from the canton of Zurich diagnosed between 1980 and 2010

	Total	SSM	NM	LMM	ALM	OTM	MNOS	*P*-value
Number	8469	3482	1393	1143	427	235	1789	
Percent		41.1	16.5	13.5	5	2.8	21.1	
Sex (%)								<0.001
Male	48.6	47	55.9	49.1	33.5	43.8	49.9	
Female	51.4	53	44.1	50.9	66.5	56.2	50.1	
Age (years)								<0.001
Median	60.3	55.1	65	71.6	58.7	62.5	58.7	
25th percentile	45.4	42.2	50.9	62.5	42.3	45.4	44.3	
75th percentile	72.7	67.5	77.3	79.3	71.3	73.9	72.6	
Location (%)								<0.001
Head and neck	17.5	7.5	19.1	53.1	2.8	16.6	16.7	
Trunk	30.8	37.9	28.3	19.7	4.9	25.1	33	
Upper limb and shoulder	22.8	25.6	26.1	16.3	19	20	20.1	
Lower limb and hip	26.4	28.1	25.8	9.3	72.6	29.4	22.8	
Multiple locations	0.01	0	0	0	0	0	0.1	
Not otherwise specified	2.5	0.9	0.7	1.6	0.7	8.9	7.3	
Breslow thickness (mm) (%)								<0.001
0–1.00	60	79	10.2	82.2	52.7	37.4	52.5	
1.01–2.00	16.5	14.8	26.9	9	19.7	14.9	15.9	
2.01–4.00	10.9	4.1	36.6	4.2	17.3	9.4	7	
>4.00	6.1	1.3	23.8	1.4	7.3	9.8	3.8	
Unknown	6.5	0.8	2.5	3.2	3	28.5	20.8	
Period (%)								<0.001
1980–1990	22.7	20.1	28.8	21.3	24.8	22.5	23.2	
1991–2000	31	33.1	31.9	33.2	33.7	34.5	23.8	
2001–2010	46.3	46.8	39.3	45.5	41.5	43	53	

ALM, acrolentiginous melanoma; LMM, lentigo maligna melanoma; MNOS, melanoma not otherwise specified; NM, nodular melanoma; OTM, other type of melanoma; SSM, superficial spreading melanoma.

Generally, the incidence of malignant melanoma increased significantly between 1980 and 2010 in both men (APC: 3.02%) and women (APC: 2.1%). The highest significant increase was observed in the period from 1980 to 1990 in both men (APC: 7.24%) and women (APC: 5.49%) (Table 2 and Fig. 1).

Observing the histological types in the period 1980–2010, there was an increasing incidence in SSM (APC: 3.24%), LMM (APC: 2.22%) and MNOS (APC: 3.24%), with statistical significance for SSM and MNOS. The incidence of the SSM subtype increased significantly in the period 1980–1990 (APC: 6.46%) and from 2001 to 2010 (APC: 7.44%). Constant incidence trends were observed for NM, ALM and OTM subtypes, although in the period from 1980 to 1990, a large significant increase was observed for NM (APC: 3.09%) and ALM (APC: 24.52%). About 92% of ALM cases were located on the limbs (391 cases), 7% were located on the trunk and head and neck (36 cases) and 1% had no specific location (three cases) (Table 2 and Fig. 2).

In terms of the location, a statistically significant APC was observed in all four locations between 1980 and 2010, with the highest increase in the upper limb and shoulder (APC: 3.57%) and the lowest increase in the lower limb and hip (APC: 1.98%). Statistically significantly increasing trends were mainly observed between 1980 and 1990 for the trunk (APC: 6.82%), upper limb and shoulder (APC: 8.31%) and the lower limb and hip (APC: 5.55%), but hardly in the following two decades. Only the incidence of the upper limb and shoulder increased statistically significantly in the period 2001–2010 (APC: 9.8%). A statistically significant increase was also observed in sun-exposed areas such as the head and neck (APC: 2.58%) (Table 2 and Fig. 3).

Table 2 Incidence trends of melanoma according to sex, subtype, size and location by time period in percent expressed as annual percent change

	Periods			
Subgroups	1980–2010	1980–1990	1991–2000	2001–2010
Sex				
Male	3.02*	7.24*	−0.59	3.78*
Female	2.10*	5.49*	1.1	3.21
Subtype				
SSM	3.24*	6.46*	−2.2	7.44*
LMM	2.22	6.66*	−2.91	3.05*
NM	0.41	3.09*	0.9	−2.78
ALM	0.8	24.52*	9.2	−8.98
OTM	0.32	11.42	−9.45	−6.24
MNOS	3.24*	2.46	4.30*	3.38*
Location				
Head and neck	2.58*	2.68	−2.91	3.05
Trunk	2.12*	6.82*	−1.77	−2.09
Upper limb and shoulder	3.57*	8.31*	0.38	9.80*
Lower limb and hip	1.98*	5.55*	0.48	2.85
Breslow thickness (mm)				
≤1.00	3.49*	8.27*	−0.97	4.67*
1.01–2.00	1.61*	−2.8	6.92	−4.81*
2.01–4.00	0.4	2.38	−0.28	1.41
>4.00	0.72	11.18*	−1.17	1.3
Unknown	0.57	−2.8	6.92	−4.81*

ALM, acrolentiginous melanoma; LMM, lentigo maligna melanoma; MNOS, melanoma not otherwise specified; NM, nodular melanoma; OTM, other type of melanoma; SSM, superficial spreading melanoma.
*Statistically significant difference ($P < 0.05$).

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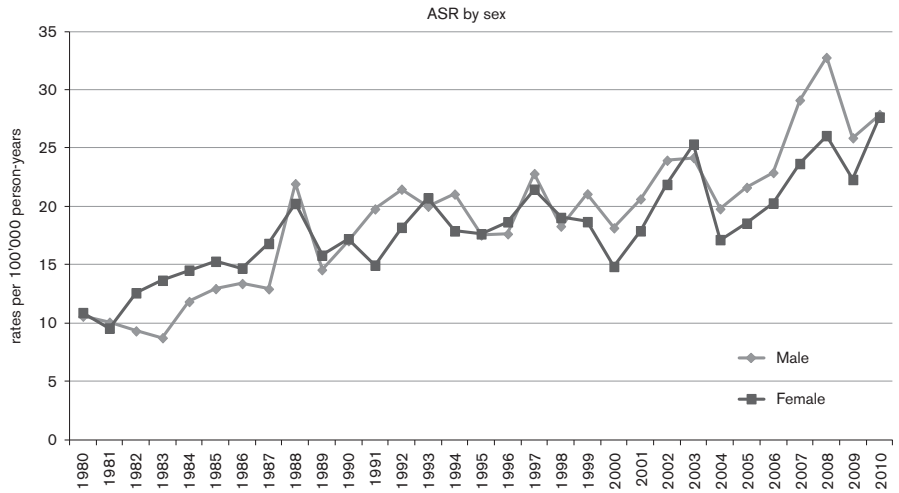
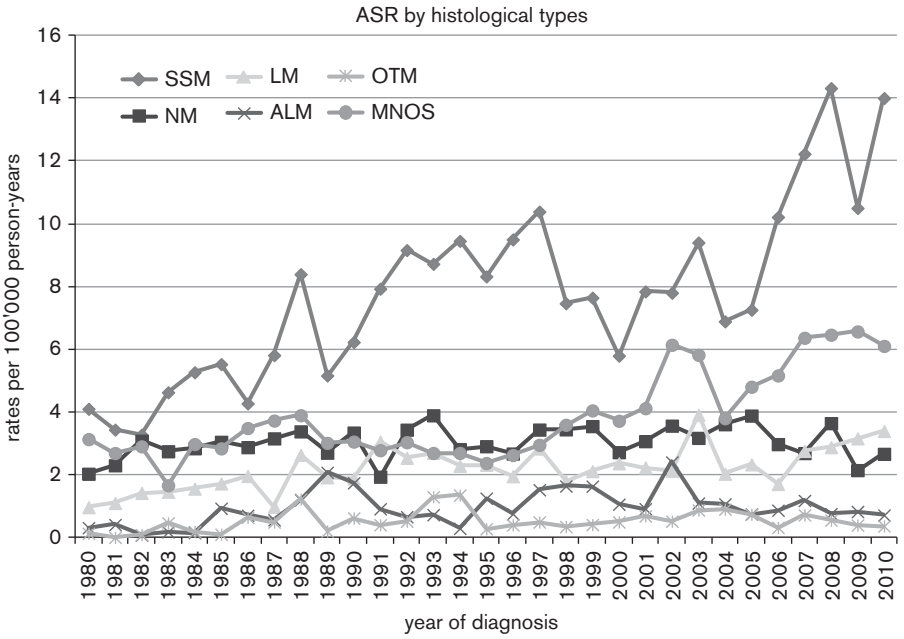
Fig. 1



Age-standardized melanoma incidence rates per 100 000 person-years by sex from 1980 to 2010, Canton of Zurich. ASR, age-standardized rates.

Fig. 2



Age-standardized melanoma incidence rates per 100 000 person-years by histological subtype from 1980 to 2010, Canton of Zurich. ALM, acrolentiginous melanoma; ASR, age-standardized rates; SSM, superficial spreading melanoma; LMM, lentigo maligna melanoma; MNOS, melanoma not otherwise specified; NM, nodular melanoma; OTM, other type of melanoma.

Observing the Breslow thickness, there was a statistically significant increase in malignant melanomas with a thickness of 1.00 mm or less (APC: 3.49%) and melanomas with a thickness of more than 1.00 mm and up to 2.00 mm (APC: 1.61%) from 1980 to 2010, whereas the incidence of melanomas with a thickness of more than 2.00 or with an unknown thickness remained almost constant. From 2001 to 2010, a statistically significant decreasing incidence was observed for melanomas with a thickness more than 1.00 mm and 2.00 mm or less (APC: −4.81%) and for melanomas with an unknown thickness (APC: −4.81%) (Table 2 and Fig. 4).

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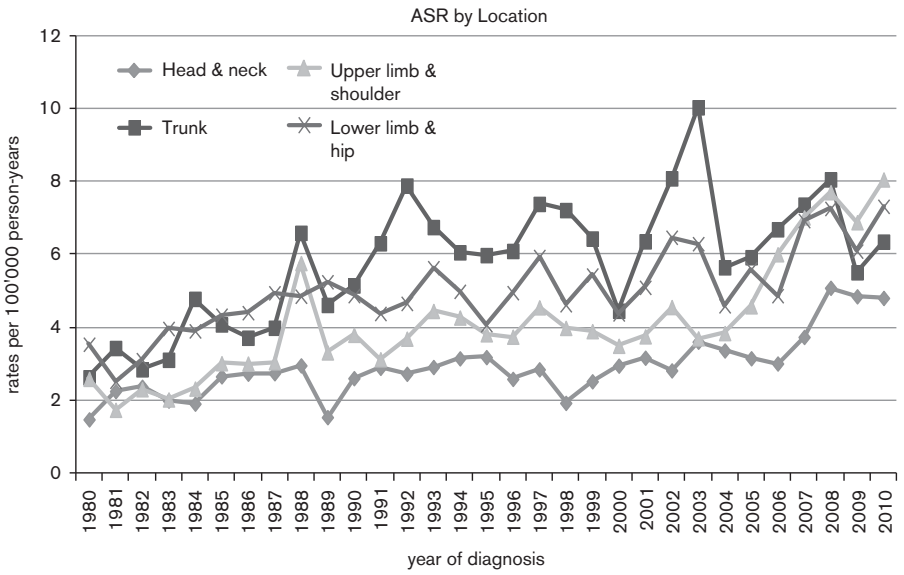
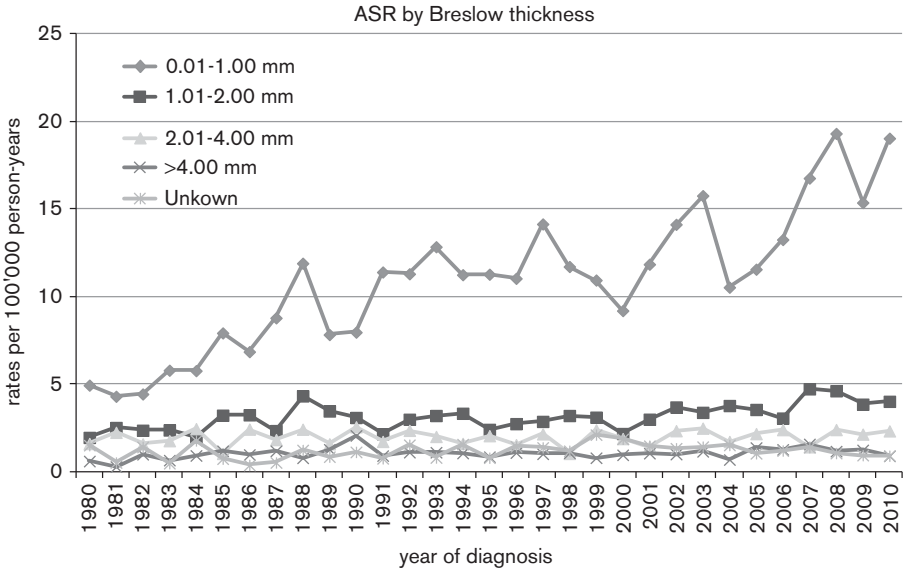
Fig. 3



Age-standardized melanoma incidence rates per 100 000 person-years by location from 1980 to 2010, Canton of Zurich. ASR, age-standardized rates.

Fig. 4



Age-standardized melanoma incidence rates per 100 000 person-years by Breslow thickness from 1980 to 2010, Canton of Zurich. ASR, age-standardized rates.

Discussion

In our analysis of data assessed in the Swiss Canton of Zurich, we observed increasing incidences of malignant melanomas in men and women between 1980 and 2010, especially in the period 1980–1990. Studies from Southern and Western Switzerland and other countries also reported an increase in the last few years and decades, especially in European countries such as Norway, Sweden, the Netherlands and Ukraine as well as the USA and Australia [19–28]. Despite the observation of a marked increase in incidence between 1980 and 1990, almost half of the cases are in the period of 2001–2010. This corresponds with the current opinion that the incidence of melanoma is still increasing.

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Overall, there were almost as many cases among men as in women, in agreement with the literature [27,29]. However, large sex-related differences were observed in the acrolentiginous subtype. In another study, similar incidence rates of these subtypes were found on comparing men and women in an analysis of US data [5].

Location analysis with the trunk as the most frequent location, followed by the lower limb and hip also corresponds with the literature, in which the trunk is the most frequent location in men and the lower limb and hip are the most frequent locations in women [20,23,27,29,30]. We expected that more than half of all LMM cases were located in the head and neck area as it is a subtype of the melanoma that occurs in places with high UV exposures over time such as the face and the neck [29]. An extraordinary observation was ALM cases located on the trunk and on the head and neck as ALM is, by definition, strictly located subungual, palmar or plantar [29]. A possible reason for these errors may be an inaccurate histological diagnosis. Otherwise, there could have been a wrong understanding of the term 'acrolentiginous' in these cases. In medical language, the term 'acral' is not only used for fingers and toes, but for other peripheral body parts such as the ears and nose. For example, a lentigo maligna melanoma on the nose could have been mistaken for an acrolentiginous melanoma. In the 1980s, there was a significant increase in the incidence of melanoma located on the trunk, upper and lower limb, whereas from 2001 to 2010, only melanoma incidence located on the upper limb increased significantly. A slight decrease was observed in melanomas of the trunk from 2001 to 2010. The increase in cases on the shoulders and upper limb in recent years has not been observed in other studies. We do not have a valid explanation for this observation, but it might be associated with leisure time and sun-bathing activities of individuals living in the canton of Zurich.

SSM was the most frequent subtype observed in the Zurich cancer registry, followed by NM, LMM and ALM, which is in agreement with the literature [20,29,31]. In our study, about 20% of all cases were 'melanomas, not otherwise specified', a similar percentage as in Southern Switzerland [20].

SSM is the only specific subtype with a significant increase in APC between 1980 and 2010, which corresponds to similar results from Southern and Western Switzerland [20,25]. In addition, we observed a significant increase in MNOS from 1980 to 2010; a study from the USA showed similar results [32].

In terms of Breslow thickness, most cases are in the category of 0.01–1.00 mm. This is also the only category for which we observed a significant increase in incidence between 2001 and 2010. The incidence rates of other categories remained almost constant or even decreased; as Breslow thickness is an important factor predicting prognosis, these rates possibly explain the constant mortality rates in Switzerland [4]. Similar results were observed in Southern Switzerland and Italy [20,24]. These results may be explained by the increased awareness and, thus, early detection. NM is a very aggressively growing form of melanoma; therefore, high percentages were found in the categories 2–4 and more than 4 mm compared with all other types. Both LMM and SSM have a very high percentage in the 0.01–1.00 mm category. A possible reason for this may be the superficial growth of these subtypes.

The median age at diagnosis was 60.3 years. It was the highest in patients with LMM; LMM usually develops from a lentigo maligna, a melanoma *in situ* occurring in sun-damaged skin [29]. In contrast, patients with the SSM or the ALM subtype were younger at diagnosis. Similar numbers and results have been found in other studies [20,29].

A strength of the data is the long time period, during which the data were registered, which allowed us to observe and analyse the incidence trends over 30 years. Another strength of the data set is the amount of information that it provides such as location, subtype and Breslow index or the distinction between melanoma *in situ* and invasive melanoma. With this information, we could carry out a precise analysis of different key aspects.

A limitation is the partially missing data on mortality, which would allow for computation of survival rates. Another limitation is that one-fifth of all melanomas were not histologically specified. The reasons for this may be case registration problems or the impossibility of identification of the subtype histologically. A limitation that is common to many evaluations of epidemiological cancer registries is the fact that we cannot examine risk factors such as family history of melanoma, skin type nor sunbathing behaviour of malignant melanomas with our database.

Conclusion

In the Swiss Canton of Zurich, the incidence of melanoma has increased over the last 30 years in both men and women. In particular, we observed an increasing incidence of SSM and thin melanomas (0.01–1.00 mm). These observations are in agreement with studies from Southern and Western Switzerland as well as other European countries and the USA [33]. The reasons for this may be the increased awareness of melanoma in the community, which leads to more frequent dermatologist consultations and earlier detection. To decrease the incidence rates, there is still a need for education on the causes of cutaneous melanoma, especially the danger of UV radiation.

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Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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